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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/755,136

01/09/2004

Diane Harris Boschelli

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EXAMINER

AULAKH, CHARANJIT

ART UNIT

PAPER NUMBER

1625

DATE MAILED: 05/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/755,136	BOSCHELLI ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,5,7,10 and 122-145 is/are pending in the application.
 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1,2,5,7,10 and 122-145 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>18</u> . | 6) <input type="checkbox"/> Other: ____ |

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DETAILED ACTION

1. According to a preliminary amendment, the applicants have canceled claims 3, 4, 6, 8, 9 and 11-121 and furthermore, have amended claims 1, 122 and 137-145.
2. Claims 1, 2, 5, 7, 10 and 122-145 are now pending in the application.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 122-145 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see *Ex parte Foreman*, 230 USPQ at 547; *Wands, In re*, 858.F.2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, the state of the prior art and the breadth of claims.

The instant compounds are inhibitors of c-Src kinase and raf kinase as shown by in vitro data on pages 122-145 of instant specification. However, there is no teaching either in the specification or prior art that increased activity of c-Src kinase or raf kinase is implicated in the etiology of every known neoplastic disease, polycystic kidney disease, restenosis, every known autoimmune disease, viral infection or osteoporosis. There is no teaching in the specification that the instant compounds will inhibit every known protein kinase in the body. There are no working examples present showing efficacy of instant compounds in known animal models of every known neoplastic disease, polycystic kidney disease, restenosis, every known autoimmune disease, viral infection or osteoporosis. It is also of note that increased activity of either c-Src kinase or raf kinase may be one of the several other known mechanisms responsible for the etiology of a particular disease condition and therefore, correcting only one mechanism will not completely cure or eradicate that disease condition. There is no teaching or guidance in the specification how the instant compounds having inhibitory effect in vitro on activity on c-Src kinase and raf kinase will have utility in treating and eradicating every known neoplastic disease, polycystic kidney disease, restenosis, every known autoimmune disease, viral infection or osteoporosis. The instant compounds of formula (I) encompasses several hundreds of thousands of compounds based on the values of variables X, A, n, R1, R2a, R2b, R2c, R3 and R4 and therefore, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to demonstrate the efficacy of instant compounds in known animal models of every known neoplastic disease, polycystic kidney disease, restenosis, every

known autoimmune disease, viral infection or osteoporosis and hence their utility for treating these conditions.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 5, 10 and 122-145 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 122 and 137-145, for the values of variables T and Z, the proviso --- provided that both T and Z are not simultaneously N ---- is not needed since T can not be N.

In claims 1, 122 and 137-145, the value of variable R1 defined as ---heteroaryl ring having 6 atoms containing 1 to 3 heteroatoms, 1 of which is N, or particularly 1 or 2 heteroatoms which may be same or different, selected from N, O and S----is indefinite since it is not clear whether N is always one of the heteroatom present in the 6-membered ring and the second heteroatom may be N, O or S or 6-membered ring can have any one of the heteroatom selected from N, O and S.

Claim 5 is a substantial duplicate of claim 1 since the values of variables T and Z are always C and N, respectively.

Claim 10 recites the limitation "aryl for the variable R1" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

In claims 122-136, the term ---neoplasms--- is indefinite since specific neoplasms are not defined.

In claims 137 and 138, the term ---kidney disease--- is indefinite since specific kidney disease is not defined.

In claim 139, the term ---disease caused by defect in a signaling pathway or by overexprerssion of a protein kinase or by dysregulated protein kinase ----- is indefinite since specific disease condition, specific signaling pathway, specific protein kinase etc. are not defined.

In claim 140, the terms ---biological effects and protein kinase ----- are indefinite since specific biological effects and specific protein kinases are not defined.

In claim 141, the term ---disease characterized by abnormal growth of cells---- is indefinite since the specific diseases are not defined.

In claim 143, the term ---autoimmune diseases--- is indefinite since specific autoimmune diseases are not defined.

In claim 144, the term ---viral infections---- is indefinite since specific viral infections are not defined.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

Art Unit: 1625

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 1, 2, 5, 7, 10 and 122-145 are rejected under 35 U.S.C. 103(a) as being obvious over Wissner (U.S. Patent no. 6,355,636).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

Wissner discloses substituted 3-cyano-[1,7] Naphthyridines as inhibitors of tyrosine kinases having utility for treating various disease conditions such as neoplastic diseases (see col. 49, lines 20-32). The exemplified compounds (see examples 57-71, 74-78,

Art Unit: 1625

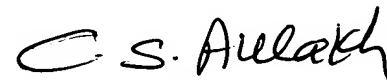
85 and 86) of Wissner are identical to the instant compounds and have identical utility except that they differ from the instant compounds in having a 6-membered aryl ring for variable R1 in the instant compounds instead of a 6-membered heteroaryl ring.

However, Wissner teaches interchangeability between an aryl group and a 6-membered heteroaryl ring (pyridine or pyrimidine) for variable X (see col. 5, line 39) which is equivalent to instant variable R1. Therefore, one skilled in the art would have been motivated to prepare the instant compounds by modifying exemplified compounds of Wissner since Wissner teaches interchangeability between a 6-membered aryl group and a 6-membered heteroaryl ring at this position without affecting their ability to inhibit tyrosine kinases and their utility of treating neoplastic diseases etc.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Charanjit S. Aulakh
Primary Examiner
Art Unit 1625